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10/526,597	10/03/2005	Shimon Slavin	U 015659-2	5790

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EXAMINER	
KIM, TAEYOON	
ART UNIT	PAPER NUMBER
1651	

NOTIFICATION DATE	DELIVERY MODE
09/17/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/526,597	SLAVIN ET AL.	
	Examiner	Art Unit	
	TAEYOON KIM	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 June 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *51,52,55-58,68,70,71 and 81-124* is/are pending in the application.

4a) Of the above claim(s) *68,70,71 and 99-105* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *51,52,55-58,81-98 and 106-124* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/15/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment and response filed on 6/11/2009 has been received and entered into the case.

Claims 1-50, 53, 54, 59-67, 69 and 72-80 are canceled, claims 106-124 are newly added, claims 68, 70, 71, 99-105 have been withdrawn from consideration as being drawn to non-elected subject matter, and claims 51, 52, 55-58, 81-98 and 106-124 are pending and have been considered on the merits. All arguments have been fully considered.

Information Disclosure Statement

The foreign patent document , JP 5-55148, which was not considered due to the lacking of English translation or the concise explanation of the relevance, is now considered, and a copy of IDS with examiner's initial is attached.

Response to Amendment

The objection to the specification has been withdrawn due to the amendment.

The claim objections have been withdrawn due to the amendment. The objection to claim 53 was made inadvertently. The claim objection was intended for claim 52 instead. See below.

The claim rejection under 35 U.S.C.§112 has been withdrawn due to the amendment.

The claim rejection under 35 U.S.C.§103 based on Cohn et al. has been withdrawn.

The claim rejection under 35 U.S.C.§103 based on Scarborough, Bentley and Maeda has been withdrawn due to a new ground of rejection based on the current amendment.

Priority

Receipt is acknowledged of papers filed under 35 U.S.C. 119 (a)-(d) based on an application filed in WIPO on 9/4/2002. Applicant has not complied with the requirements of

37 CFR 1.63(c), since the oath, declaration or application data sheet does not acknowledge the filing of any foreign application. A new oath, declaration or application data sheet is required in the body of which the present application should be identified by application number and filing date.

Claim Objections

Claim 52 is objected to because of the following informalities: The term "morphogenetic" appears to be "morphogenic". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 88-98, 106, 108, 111-113, 115, 116 and 120-122 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The current application generically claims any responsive polymeric system comprising site-responsive RTG biodegradable polymer, however the specification does not contain an adequate description for the entire scope of this limitation and thus the claims. The claims are not limited to a particular species just generically any responsive polymeric system comprising site-responsive RTG biodegradable polymer which is known in the art and those which have not been isolated and/or identified including variants of known biodegradable RTG polymer. The written

description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. See Eli Lilly, 119 F.3d at 1568,43 USPQ2d at 1406.

The claims are essentially of limitless breadth. It is implied that so long as the specification provides one with the ability to test any particular embodiment which is encompassed by the material limitations of a claim, one can thereby distinguish between those embodiments which meet the functional limitations from those embodiments which don't. This argument is not entirely without merit. However, the issue here is the breadth of the claims in light of the predictability of the art as determined by the number of working examples, the skill level of the artisan and the guidance presented in the instant specification and the prior art of record. This 'make and test' position is inconsistent with the decisions in In re *Fisher,* 427 F.2d 833,166

Every species in a genus need not be described in order that a genus meets the written description requirement. See Utter, 845 F.2d at 998- 99,6 USPQ2d at 1714 ("A specification may, within the meaning of §112, first paragraph, contain a written description of a broadly claimed invention without describing all species that claim encompasses.") In claims to a species from a genus, however, a generic statement without more, is not an adequate written description of the genus because it does not distinguish the claimed species of the genus from others. One

skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, does not suffice to define the genus because it is only an indication of what the genus does, rather than what it is. See Fiers, 984 F.2d at 1169-71, 25 USPQ2d at 1605- 06 (discussing Amgen). It is only a definition of a useful result rather than a definition of what achieves that result. Many such species of the genus may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re *Wilder*, 736 F.2d 1516, 1521, 222 USPQ 369,372- 73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally thought to exist, in the absence of knowledge as to what that material consists of, is not a description of that entire material.

The instant specification discusses various biodegradable polymers (p.10). However, the specification only discloses one example of biodegradable reverse thermo-responsive polymers citing Cohn et al. (J. Mat. Sci. Mater. Med. 2003) (p.20). According to Cohn et al., the biodegradable RTG comprises poly(ether carbonate). The specification discloses such RTG polymer comprising poly(ether carbonate) (i.e. [PEG6000-O-CO-O-PPG3000]n poly(ether carbonate))(p.33 and 55). The specification also discloses [-PEG6000-O-CO-(CH2)4-CO-O-PPG3000] poly(ether-ester) (p. 33). However, these two examples are not considered to represent the entire scope of the biodegradable RTG polymer as claimed instantly.

Furthermore, claim 89 discloses the limitation of "RTG polymer comprising at least one silicon-containing reactive group". Since claim 89 is dependent on claim 88, the RTG polymer of

claim 89 is also considered to be biodegradable. However, the specification did not disclose whether the examples of RTG polymers containing silicon-containing reactive group (e.g. F127 di-IPTS, p.56; F38 di-IPTS, p.56; PEG400 di-IPTS, etc.). According to Bentley et al., poloxamers which comprise pluronics are not biodegradable (see par. 8). Therefore, some of examples in the specification of the instant application, which contain pluronics such as F127 or F38 are not considered to be biodegradable.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 51, 52, 55-58, 63, 67, 81-88, 90-98, 107-117, and 124 are rejected under 35 U.S.C. 103(a) as being unpatentable over Scarborough (of record) in view of Krezanoski (US 4,188,373) and Bentley et al. (of record).

Scarborough teaches a composition comprising bone marrow cells (BMC), demineralized bone matrix (DBM), which can be in a powder format (par. 17; claims 85 and 95), and reverse phase block copolymers or pluronics (par. 5 and 17-21).

The reverse phase polymer of Scarborough is considered as reverse thermal gels or reverse thermo-gelating (RTG) polymers since "reverse phase block copolymer" is interchangeable to "reverse thermo-gelating polymer" in the art. Furthermore, the pluronics of Scarborough (see par. 20 and 21) is well known in the art as the RTG since the polymers can form a gel at body temperature according to Krezanoski (see col. 4, line 32 through col. 5, line 42).

Still further, the reverse phase block copolymer or Pluronics of Scarborough is polymers

having a property of sol-gel transition at a certain temperature, and such transition would inherently increase viscosity at least two folds and the condensation of water and polymer during the transition would inherently increase the molecular weight of the gelling polymers due to the water contents in gels. Thus, Scarborough meets the limitation of claim 51.

Scarborough does not teach the RTG or reverse phase block copolymer is biodegradable (claim 88).

Bentley et al. teach biodegradable RTG such as poly(ether carbonate) comprising PEO $[(CH_2CH_2O)_n]$ and PPO $[(CHR^1CHR^2O)_n$, when R^1 is H, R^2 is alkyl such as methyl $(CH_3)]$ (par. 12-19).

It would therefore have been obvious for the person of ordinary skill in the art at the time the invention was made to use poly(ether carbonate) of Bentley et al. as a reverse phase block copolymer used as a carrier for bone materials.

The skilled artisan would have been motivated to make such a modification because Scarborough teaches the use of reverse phase block copolymers as a carrier of the bone composition, and the poly(ether carbonate) of Bentley et al. is such a copolymer having reverse thermo gelling capability, a person of ordinary skill in the art would recognize that the poly(ether carbonate) of Bentley et al. can be used for the carrier of bone composition. Furthermore, Bentley et al. teach that the poly(ether carbonate) can be used as an implantable gel delivery system and surgical implants (par. 84, 86, 109), and thus the poly(ether carbonate) of Bentley et al. is a suitable option to be used for the carrier of bone composition of Scarborough.

The person of ordinary skill in the art would have had a reasonable expectation of success in using poly(ether carbonate) of Bentley et al. as a carrier for the bone composition comprising

BMC and DBM of Scarborough.

Scarborough also teach powdered bone or bone particles being in average particle size from about 0.1 to about 1.2 cm (par. 14), and thus meets the limitation of claims 96.

Scarborough also teaches that the composition comprises bone morphogenic proteins (BMPs) (claim 52) as well as growth factors (par. 17)(claim 81).

With regard to the limitations in claims 55-58 are drawn to the properties of the block copolymer undergoing transition in response to a triggering effect such as temperature, the RTG/reverse phase block copolymer or Pluronics of Scarborough inherently meets the limitations since Krezanoski teaches that the Pluronics are examples of polymers which are polyoxyethylene-polyoxypropylene block copolymers having a sol-gel transition temperature in the range of from about 25°C to about 40°C (col. 4, line 32 through col. 5, line 42). Furthermore, the RTG polymer of Bentley et al. inherently meets the limitations since Bentley et al. teach the sol-gel transition of the poly(ether carbonate) being reversible such that gel is formed at 37°C (body temperature) and it becomes a free-flowing liquid at 4°C (par. 13 and 126).

With regard to the limitation drawn to the amount of BMCs (claims 83 and 93), the ratio between BMC and DBM (claims 87, 97 and 109-112), the ratio between BMC-DBM mixture and RTG polymer (claim 98, 121 and 122), or the particle size of DBM (claims 114 and 115), the references are silent. However, it would have been obvious to a person of ordinary skill in the art to optimize the number of BMCs or the ratio of BMC and DBM to obtain optimal results from the using of the composition of Scarborough in view of Krezanoski.

This is because a person of ordinary skill in the art would recognize that the amount of BMCs, the ratio between BMC and DBM or the ratio between BMC-DBM mixture and RTG

polymer is a result-effective variable. The variables would be routinely optimized by one of ordinary skill in the art in practicing the invention disclosed by those references.

With regard to the limitations drawn to the origin of DBM (claims 84, 94 and 108), although Scarborough in view of Bentley et al. do not particularly teach the limitations, it would have been obvious to a person of ordinary skill in the art to try human BMCs since the composition is used for treating osteoporosis in vertebrate animals (par. 6 and 11).

With regard to the limitation of claim 90 drawn to the polymer being a linear, the RTG polymer of Bentley et al. is typically a linear polymer (par. 65).

With regard to the limitation of claim 91 drawn to the polymer further comprising additional reactive groups such as double bond-containing reactive groups, Bentley et al. teach reactive groups can be alkenyl (double bond containing group) (par. 62).

Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill at the time the invention was made.

Claims 88, 89, 106 and 118-120 are rejected under 35 U.S.C. 103(a) as being unpatentable over Scarborough (supra) in view of Bentley et al. (of record) in further view of Orefice et al. (2000, J. Braz. Chem. Soc.) and Witucki (1993; J. Coat. Tech.).

Scarborough in view of Bentley et al. teaches the limitation of claim 88 (see above).

Scarborough in view of Bentley et al. does not teach the limitation of the limitation of claims 89, 106 and 118-120 drawn to the RTG polymer having silicon-containing reactive group.

Orefice et al. teach polymeric matrices reinforced with alkoxysilane species such as aminopropyl triethoxysilane or isocyanatopropyl triethoxysilane by chemically modifying

polymer surfaces through the introduction of special alkoxysilane groups (Abstract; p.80, left col.).

It would therefore have been obvious for the person of ordinary skill in the art at the time the invention was made to try to modify the RTG polymer of Scarborough in view of Bentley et al. with the method of Orefice et al.

The skilled artisan would have been motivated to make such a modification because Orefice et al. teach that the introduction of alkoxysilane group (silicon-containing reactive group) to the bioactive polymers enhances cell adhesion (entire document), and thus a person of ordinary skill in the art would recognize that the presence of silicon-containing reactive group would be beneficial providing better adhesion to the bone marrow cells present in the composition of Scarborough in view of Bentley et al. for treating bone. promote cell adhesion to the polymers.

With regard to the limitation directed to the reactive group being a mono-, di- or tri-functional group, the limitation is considered as an optional choice known in the art and it is extremely well known in the art that alkoxysilane can have mono-, di- or trifunctional groups based on the number of reactive residues. According to Witucki, alkoxy silane can be formulated as

$$R_n\text{-Si-}X_{4-n}$$

where R is a nonhydrolyzable organic moiety that can be an alkyl, aromatic, organofunctional, or a combination of any of these groups, and X is an alkoxy moiety, most typically methoxy or ethoxy, which reacts with the various forms of hydroxyl groups and liberates methanol or ethanol. These groups can provide the linkage with inorganic substrates, pigment, or filler to

improve coating integrity and adhesion. The methoxy groups are also capable of reacting with hydroxy functional polymers (p.1, right col.).

Thus, it would have been obvious to a person of ordinary skill in the art to try silicon-containing reactive group having different number of functional groups based on desired surface modification onto the silicon-containing reactive group.

Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill at the time the invention was made.

Response to Arguments

Applicant's arguments have been considered but are moot in view of the new ground(s) of rejection.

However, the Examiner wishes to point out that the argument made by the applicant with regard to the previous 35 U.S.C.§103 rejection based on Scarborough in view of Bentley et al. since the same reference is cited in the current claim rejection.

First, applicant indicated that the previous office action did not address claim 88. This is not correct. The limitation of claim 88 is directed to a composition comprising BMC, DBM and site-responsive reverse thermo-gelating polymer. As discussed in the previous OA under 35 U.S.C.§103 based on Scarborough (see p.6 of the previous OA mailed on 12/11/08), Scarborough teaches BMC, DBM and reverse phase block copolymer, which is considered as RTG polymer, and this teaching of Scarborough renders the limitation of claim 88 obvious.

Applicant alleged that the composition taught by Scarborough may be found in the reference only if one cherry-picks the third out of three possibilities suggested for bone material, the fourth out of 10 possibilities suggested for carriers and second example provided for the 27th

out of 51 possibilities suggested for medically/surgically useful agents. Applicant further alleged that there is no teaching or suggestion whatsoever to pick the one that the office action states it teaches.

This argument is not persuasive. Since the components of the composition claimed in the instant application are taught by the cited reference, it would have been obvious to a person of ordinary skill in the art to choose components from the listed species of Scarborough.

The species listed in Scarborough are taught to be present in the composition of Scarborough, and Scarborough does not need to provide any working examples comprising bone marrow cells. The teaching of Scarborough clearly suggests picking and choosing any of the listed species including bone marrow cells (par. 18 of Scarborough) to be used for the bone composition.

The argument based on "at once envisage" is improperly used. Applicant is reminded that the claim rejection is under 35 U.S.C.§103 rather than 102.

With regard to the argument based on M.P.E.P. §2144.08 stating "The fact that a claimed species or subgenus is encompassed by a prior art genus is not sufficient by itself to establish a prima facie obviousness". This is not persuasive since Scarborough discloses species for the claimed invention. Scarborough clearly teaches bone marrow cells, demineralized bone matrix, and reverse phase block copolymer or Pluronics.

Applicant alleged that Bentley's polymers do not have the feature of "capable of undergoing a condensation reaction in the presence of water resulting in an increase in the molecular weight of the polymeric system", and applicant also cited a paragraph disclosed by Bentley et al. and concluded that the paragraph teaches the opposite feature. This argument is

based on improper analysis of Bentley et al. First of all, any RTG polymer going through sol-gel transition in the presence of water meets the limitation. The polymers of Bentley et al. are formulated to overcome non-biodegradable nature of poloxamer (i.e. pluronics) by introducing a hydrolysable linkage such as poly(ether carbonate). The nature of sol-gel transition of Bentley et al.'s polymer is not changed and thus, the polymer of Bentley et al. inherently possesses the feature of RTG polymer, which is "capable of undergoing a condensation reaction in the presence of water resulting in an increase in the molecular weight of the polymeric system". Furthermore, pluronics as taught by Scarborough is shown as an example in the specification of current application.

The cited paragraph of Bentley et al. describes biodegradability of the polymer via hydrolysis of the polymer after sol-gel transition. Applicant misinterpreted the teaching as if the significantly lower molecular weight than the starting polymer is meant to be sol-gel transition. What the paragraph teaches is that once sol-gel transition is complete, the resulting polymer would be degradable hydrolytically to smaller soluble oligomer.

With regard to the limitation of "silicon-containing reactive groups", applicant argued that the silicones suggested by Scarborough do not contain any silicon-containing reactive groups. Based on the new ground of rejection, this argument is moot.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TAEYOON KIM whose telephone number is (571)272-9041. The examiner can normally be reached on 8:00 am - 5:00 pm ET (Mon-Thu).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Taeyoon Kim/
Primary Examiner, Art Unit 1651